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AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for reducing amyloid plaque burden in a mammal comprising effecting presentation to said mammal's immune system of an immunogenically effective amount of an analogue of said mammal's autologous A $\beta$  or autologous APP wherein is introduced at least one isolated foreign T helper epitope by means of insertion, addition, deletion, or substitution, ~~or by means of separate coupling to a polyhydroxypolymer carrier backbone of said foreign T helper epitope~~ wherein said foreign T helper epitope is selected from a group consisting of Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagglutinin epitope, a *P. falciparum* CS epitope and an artificial MHC-II binding peptide sequence; ~~and an A $\beta$  or APP derived peptide sequence wherein said sequence is selected from the group consisting of amino acids 700-714 of SEQ ID NO:2 and amino acids 672-714 of SEQ ID NO:2,~~ whereby immunization of said mammal with said analogue induces production of antibodies against the autologous A $\beta$  or autologous APP in said mammal.

2. (Cancelled)

3. (Previously Presented) The method according to claim 1, wherein the introduction further comprises:

- at least one first moiety which is a specific binding partner, selected from the group consisting of a hapten and a carbohydrate, for a B-lymphocyte specific surface antigen or an antigen presenting cell (APC) specific surface antigen, which targets the analogue to an antigen presenting cell (APC) or a B-lymphocyte,
- at least one second moiety selected from the group consisting of a cytokine, heat shock protein or hormone, which, stimulates the immune system, and/or
- at least one third moiety selected from the group consisting of a lipid and a polyhydroxypolymer, which optimizes presentation of the analogue to the immune system.

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4. (Previously Presented) The method according to claim 3, wherein the analogue is modified by introducing side groups, by covalent or non-covalent binding to suitable chemical groups in A $\beta$  or APP, or a subsequence thereof, of the first and/or of the second and/or of the third moiety.
5. (Cancelled)
6. (Cancelled)
7. (Previously Presented) The method according to claim 1, wherein introduction of the amino acid substitution, deletion, insertion and/or addition results in a substantial preservation of the overall tertiary structure of A $\beta$  or APP.
8. (Previously Presented) The method according to claim 1, wherein the analogue includes a duplication of at least one B-cell epitope of the amyloidogenic polypeptide and/or an introduction of a hapten.
9. (Currently Amended) The method according to claim 1, wherein the foreign T-cell epitope is immunodominant in the mammal.
10. (Previously Presented) The method according to claim 1, wherein the foreign T-cell epitope is promiscuous.
11. (Cancelled)
12. (Cancelled) The method according to claim 3, wherein the first moiety is selected from a substantially specific binding partner for a B-lymphocyte specific surface antigen and a substantially specific binding partner for an APC specific surface antigen.
13. (Cancelled) The method according to claim 3, wherein the second moiety is selected from a cytokine, a hormone, and a heat-shock protein.

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14. (Cancelled) The method according to claim 3, wherein the third moiety is a lipid or wherein the third moiety is a polyhydroxypolymer.

15. (Cancelled)

16. (Cancelled)

17. (Previously Presented) The method according to claim 1, wherein the autologous A $\beta$  or APP has been modified so as to preserve B-cell epitopes which are not exposed to the extracellular phase when present in a cell-bound form of the autologous APP.

18. (Previously Presented) The method according to claim 17, wherein the autologous A $\beta$  or APP has been modified so as to lack at least one B-cell epitope which is exposed to the extracellular phase when present in a cell-bound form of the autologous APP.

19. (Previously Presented) The method according to claim 1 which comprises a substitution of at least one amino acid sequence within autologous A $\beta$  or APP with an amino acid sequence of equal or different length which gives rise to a foreign T<sub>H</sub> epitope in the analogue.

20. (Cancelled)

21. (Cancelled)

22. (Cancelled)

23. (Cancelled)

24. (Cancelled)

25. (Previously Presented) The method according to claim 1, wherein presentation to the immune system is effected by having at least two copies of the analogue covalently or non-covalently linked to a carrier molecule capable of effecting presentation of multiple copies of antigenic determinants.

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26. (Previously Presented) The method according to claim 1, wherein the analogue has been formulated with an adjuvant which facilitates breaking of autotolerance to autoantigens.

27. (Previously Presented) The method according to claim 1, wherein an effective amount of the analogue is administered to the animal via a route selected from the parenteral route; the peritoneal route; the oral route; the buccal route; the sublingual route; the epidural route; the spinal route; the anal route; and the intracranial route.

28. (Previously Presented) The method according to claim 27, wherein the effective amount is between 0.5  $\mu$ g and 2,000  $\mu$ g of the analogue.

29. (Previously Presented) The method according to claim 27, wherein the analogue is contained in a virtual lymph node (VLN) device.

Claims 30-32 (Cancelled)

33. (Previously Presented) The method according to claim 1, which includes at least one administration per year.

Claims 34-58 (Cancelled)

59. (Previously Presented) The method according to claim 10, wherein the foreign T-cell epitope is selected from a natural promiscuous T-cell epitope and an artificial MHC-II binding peptide sequence.

60. (Currently Amended) The method according to claim 1, wherein the tetanus toxoid epitope is selected from the group consisting of SEQ ID NO: 4 and SEQ ID NO: 6.

61. (Cancelled) The method according to claim 12 wherein the specific binding partner is selected from a group consisting of a hapten and a carbohydrate for which there is a receptor on the B-lymphocyte or the APC.

62. (Previously Presented) The method according to claim 3, wherein the cytokine is selected from the group consisting of interferon  $\gamma$ , Flt3L, interleukin 1, interleukin 2, interleukin 4,

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interleukin 6, interleukin 12, interleukin 13, interleukin 15, and granulocyte-macrophage colony stimulating factor.

63. (Previously Presented) The method according to claim 3, wherein the heat shock protein is selected from the group consisting of HSP70, HSP90, HSC70, GRP94, and calreticulin.

64. (Previously Presented) The method according to claim 3, wherein the third moiety is a lipid selected from the group consisting of a palmitoyl group, a myristyl group, a farnesyl group, a geranyl-geranyl group, a GPI-anchor, and an N-acyl diglyceride group.

65. (Previously Presented) The method according to claim 3, wherein the polyhydroxypolymer is a polysaccharide.

66. (Previously Presented) The method according to claim 33, comprising at least 2 administrations per year.

67. (Previously Presented) The method according to claim 66, comprising at least 3 administrations per year.

68. (Previously Presented) The method according to claim 27, wherein the parenteral route is selected from the group consisting of the subcutaneous, the intracutaneous, and the intramuscular route.

69. (Previously Presented) The method according to claim 1, wherein the artificial MHC-II binding peptide sequence is the amino acid sequence of SEQ ID NO. 19.

70. (Cancelled)

71. (Previously Presented) A method for reducing amyloid plaque burden in a mammal, the method comprising:

-administering an immunogenically effective amount of at least one modified A $\beta$  or APP polypeptide, wherein said modified A $\beta$  or APP polypeptide differs from the mammal's autologous A $\beta$  or autologous APP polypeptide in that it comprises at least one isolated foreign T helper epitope selected from the group consisting of a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus

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hemagglutinin epitope, a *P. falciparum* CS epitope and an artificial MHC-II binding peptide sequence

whereby administration to said mammal with said modified A $\beta$  or APP polypeptide induces production of antibodies against the autologous A $\beta$  or autologous APP polypeptide in said mammal.

72. (Currently Amended) The method according to ~~claim 70~~ or claim 71, wherein said modified A $\beta$  or APP polypeptide further comprises:

- at least one first moiety which is a specific binding partner, selected from the group consisting of a hapten and a carbohydrate, for a receptor on a B-lymphocyte or an antigen presenting cell (APC), which targets the modified A $\beta$  or APP polypeptide to an antigen presenting cell (APC) or a B-lymphocyte, and/or
- at least one second moiety selected from the group consisting of a cytokine, heat shock protein or hormone, which stimulates the immune system, and/or
- at least one third moiety selected from the group consisting of a lipid and a polyhydroxypolymer, which optimizes presentation of the modified A $\beta$  or APP polypeptide to the immune system.

73. (Cancelled)

74. (Previously Presented) A method for reducing amyloid plaque burden in a mammal, the method comprising:

-administering an immunogenically effective amount of at least one modified A $\beta$  or APP polypeptide, wherein said modified A $\beta$  or APP polypeptide differs from the mammal's autologous A $\beta$  or autologous APP polypeptide in that it comprises at least one isolated foreign T helper epitope selected from the group consisting of a

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Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagglutinin epitope, a *P.falciparum* CS epitope and a pan DR epitope peptide

whereby administration to said mammal with said modified A $\beta$  or APP polypeptide induces production of antibodies against the autologous A $\beta$  or autologous APP polypeptide in said mammal.

75. (Previously Presented) The method according to ~~claim 73 or~~ claim 74, wherein the modification further comprises:

- at least one first moiety which is a specific binding partner, selected from the group consisting of a hapten and a carbohydrate, for a receptor on a B-lymphocyte or an antigen presenting cell (APC), which targets the modified A $\beta$  or APP polypeptide to an antigen presenting cell (APC) or a B-lymphocyte, and/or
- at least one second moiety selected from the group consisting of a cytokine, heat shock protein or hormone, which stimulates the immune system, and/or
- at least one third moiety selected from the group consisting of a lipid and a polyhydroxypolymer, which optimizes presentation of the modified A $\beta$  or APP polypeptide to the immune system.

76. (Currently Amended) A method for reducing amyloid plaque burden in a mammal comprising effecting presentation to said mammal's immune system of an immunogenically effective amount of an analogue of said mammal's autologous A $\beta$  or autologous APP wherein is introduced at least one isolated foreign T helper epitope by means of insertion, addition, deletion, or substitution, ~~or by means of separate coupling to a polyhydroxypolymer carrier backbone of said foreign T helper epitope,~~ wherein said foreign T helper epitope is selected from a group consisting of Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagglutinin epitope, a *P.falciparum* CS epitope and a pan DR epitope peptide; ~~and an A $\beta$  or APP derived peptide sequence wherein said sequence is selected from the group consisting of amino acids 700-714 of SEQ ID NO:2 and amino acids 672-714 of SEQ ID NO:2,~~ whereby

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immunization of said mammal with said analogue induces production of antibodies against the autologous A $\beta$  or autologous APP in said mammal.

77. (New) A method according to claim 1, wherein the analogue is selected from the group consisting of

- three identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope,
- nine identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope, - amino acids 672-714 of SEQ ID NO: 2 having an isolated foreign T helper epitope fused to the N- or C-terminus;
- amino acids 672-714 of SEQ ID NO: 2 wherein has been introduced an isolated foreign T helper epitope by means of substitution;
- amino acids 672-714 of SEQ ID NO: 2, wherein has been introduced an isolated foreign T-helper epitope by means of insertion,
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 714-770;
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 714-770; and
- amino acids 630-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 630-672; and
- amino acids 630-714 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 630-672.

78. (New) A method according to 71, wherein the modified A $\beta$  or APP polypeptide is selected from the group consisting of

- three identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope,



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- nine identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope, - amino acids 672-714 of SEQ ID NO: 2 having an isolated foreign T helper epitope fused to the N- or C-terminus;
- amino acids 672-714 of SEQ ID NO: 2 wherein has been introduced an isolated foreign T helper epitope by means of substitution;
- amino acids 672-714 of SEQ ID NO: 2, wherein has been introduced an isolated foreign T-helper epitope by means of insertion,
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 714-770;
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 714-770; and
- amino acids 630-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 630-672; and
- amino acids 630-714 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 630-672.

79. (New) A method according to 74, wherein the modified A $\beta$  or APP polypeptide is selected from the group consisting of

- three identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope,
- nine identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope, - amino acids 672-714 of SEQ ID NO: 2 having an isolated foreign T helper epitope fused to the N- or C-terminus;
- amino acids 672-714 of SEQ ID NO: 2 wherein has been introduced an isolated foreign T helper epitope by means of substitution;

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- amino acids 672-714 of SEQ ID NO: 2, wherein has been introduced an isolated foreign T-helper epitope by means of insertion,
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 714-770;
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 714-770; and
- amino acids 630-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 630-672; and
- amino acids 630-714 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 630-672.

80. (New) A method according to 76, wherein the modified A $\beta$  or APP polypeptide is selected from the group consisting of

- three identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope,
- nine identical APP fragments consisting of amino acids 672-714 of SEQ ID NO: 2 separated by the at least one isolated foreign T helper epitope, - amino acids 672-714 of SEQ ID NO: 2 having an isolated foreign T helper epitope fused to the N- or C-terminus;
- amino acids 672-714 of SEQ ID NO: 2 wherein has been introduced an isolated foreign T helper epitope by means of substitution;
- amino acids 672-714 of SEQ ID NO: 2, wherein has been introduced an isolated foreign T-helper epitope by means of insertion,
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 714-770;
- amino acids 672-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 714-770; and

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- amino acids 630-770 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of substitution into amino acids 630-672;  
and
- amino acids 630-714 of SEQ ID NO: 2 wherein has been introduced at least one isolated foreign T helper epitope by means of insertion into amino acids 630-672.